The hyperaggregability of platelets from normal pregnancy is mediated through thromboxane A2 and cyclic AMP pathways

許準榕
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Abstract

There is substantial evidence of increased platelet reactivity in vivo and in vitro during pregnancy, with the risk of developing pre-eclampsia. In this study, platelet function was studied during 28-40 weeks of gestation in a group of women who remained normotensive and in a group of nonpregnant female controls. Platelet aggregation stimulated by thrombin and adenosine diphosphate was markedly enhanced in washed platelets from pregnant subjects. Thrombin (0.04 U/ml)-evoked increases in intracellular Ca+2 mobilization of Fura 2-AM-loaded platelets were also enhanced in pregnant subjects. The binding of fluorescein isothiocyanate (FITC)-triflavin (2 microg/ml) to the glycoprotein IIb/IIIa complex in thrombin-activated platelets did not differ significantly between the nonpregnant and pregnant groups. Thromboxane A2 (TXA2) formation in both resting and thrombin-activated platelets from pregnant subjects was significantly greater than from nonpregnant subjects. Levels of cyclic adenosine monophosphate (cAMP) in both resting and prostaglandin E1-treated platelets (10 micromol/l) from pregnant subjects were significantly lower than those from nonpregnant subjects. There were no significant differences between nonpregnant and pregnant subjects in platelet cAMP levels in the presence of imidazole (600 micromol/l) and indomethacin (500 micromol/l). Intracellular pH values in platelets were measured spectrofluorometrically using the fluorescent probe, BCECF-AM. The increase in intracellular pH stimulated by thrombin (0.04 U/ml) in pregnant subjects was markedly greater than that in observed nonpregnant subjects. We conclude that the agonist-induced hyperaggregability of platelets in normal pregnancy may be due, at least partly, to stimulation of the Na+/H+ exchanger and subsequently to elevated intracellular Ca+2 mobilization, and then to increased TXA2 formation and a lowered level of cAMP, which leads to further increases in intracellular Ca+2 mobilization, and finally to enhanced platelet aggregation.